IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:

McKENZIE et al.

Serial No.: 09/163,089

Filed: September 29, 1998

Atty. File No.: 5036-1

For: COMPOSITIONS FOR IMMUNOTHERAPY AND USES THEREOF

Group Art Unit: 1645

Examiner: Zeman, R.

PETITION TO WITHDRAW HOLDING OF ABANDONMENT
(37 CFR 1.181(a))

CERTIFICATE OF MAILING

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO THE COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450 ON 11/30/04

SHERIDAN ROSS P.C.

BY: Kathleen Mahnush

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This Petition to Withdraw Holding of Abandonment under 37 CFR 1.181(a) is submitted in response to a Notice of Abandonment mailed on November 3, 2004, for the above-identified patent application. The Notice of Abandonment mailed November 3, 2004 stated that Applicants had failed to timely file a proper reply to the Office letter mailed on 26 April 2004.

Applicants submit that the Patent Office is in error in stating that Applicants failed to timely file a proper reply to the 26 April 2004 Office letter, which was a final Office Action.

The facts supporting Applicants' position are as follows. On October 20, 2004, Applicants filed with the United States Patent Office using the Certificate of Mailing procedure, the following documents: (1) an Amendment and Response to the April 26 Office Action; (2) a Request for a three month extension of time, to extend the time for responding from July 26, 2004 to October 26, 2004; (3) a check in the amount of $490 as payment of the three month extension fee; and (4) a return postcard. A copy of each of the above-identified documents is attached hereto as Appendix A.

The United States Patent Office acknowledged receipt of the above-identified documents on October 27, 2004 by a receipt-dated stamp on the return postcard. Moreover, the U.S. Patent Office PAIR system shows a "Workflow Incoming Amendment IFW" on October 27, 2004. A copy of the stamped return postcard and the PAIR website printout are attached hereto as Appendix B.

On October 26, 2004, Applicants filed with the United States Patent Office using the Certificate of Mailing procedure, the following documents: (1) A Notice of Appeal; (2) a check in the amount of $170 as payment of the Notice of Appeal fee; and (3) a return postcard. A copy of each of the above-identified documents is attached hereto as Appendix C.

The United States Patent Office acknowledged receipt of the documents in Appendix C by a receipt-dated stamp on the return postcard. A copy of the stamped return postcard is attached hereto as Appendix D.

In view of the foregoing facts and the attached supporting documentation, Applicants submit that the required reply in response to the 26 April 2004 Office Action, including a Notice of Appeal, was timely and properly filed and was received by the United States Patent Office. Applicants therefore respectfully request that the Examiner withdraw the holding of abandonment for the above-identified patent application, and allow the application to continue in prosecution.

No additional fees are believed to be due in connection with this Petition to Withdraw Holding of Abandonment, but in the event that fees are due, please debit Deposit Account No. 19-1970.

Respectfully submitted,

SHERIDAN ROSS P.C.

By: Angela Sebor

Angela Dallas Sebor
Registration No. 42,460
1560 Broadway, Suite 1200
Denver, CO 80202-5141
(303) 863-9700

Date: November 30, 2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:

McKENZIE et al.

Serial No.: 09/163,089

Filed: September 29, 1998

Atty. File No.: 5036-1

For: "COMPOSITIONS FOR IMMUNOTHERAPY AND USES THEREOF"

Group Art Unit: 1645

Examiner: Zeman, R.

REQUEST FOR EXTENSION OF TIME

CERTIFICATE OF MAILING

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO THE COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450 ON 10/20/04.

SHERIDAN ROSS P.C.

BY: Kathleen Mackinnis

M.S. AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicants, through their attorneys, respectfully petition for an extension of time under 37 CFR § 1.136(a) of three (3) months to respond to the Office Action mailed on April 26, 2004, with respect to the above-identified application, thereby extending the period for response from July 26, 2004, to October 26, 2004.

Enclosed is a check in the amount of $490 as payment for the extension fee. Please credit any overpayment or debit any underpayment to Deposit Account No. 19-1970.

Respectfully submitted,

SHERIDAN ROSS P.C.

By: Angela Sebor

Angela Dallas Sebor
Registration No. 42,460
1560 Broadway, Suite 1200
Denver, CO 80202-5141
(303) 863-9700

Date: October 20, 2004

22531

SHERIDAN ROSS F
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DENVER, CO 80274
23-7-1020

DATE	CHECK NO	CHECK AMOUNT
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COMMISSIONER OF PATENTS AND TRADEMARKS

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SHERIDAN ROSS AUTHORIZED SIGNATURE

"022531" 1:10200075:2016521796"

SHERIDAN ROSS

VENDOR NO. 22531 VENDOR NAME

TRANSACTION DATE	REFERENCE	GROSS AMOUNT	DEDUCTION	NET AMOUNT
10/20/04	OPER-KB	Petition for Extension of Time 5036-1	1122000	490.00

CHECK DATE	CHECK NO.	TOTAL GROSS	TOTAL DEDUCTION	CHECK AMOUNT
10/20/04	22531			490.00

Initial: km

Date 10/20/04

PTO Stamp indicates receipt of: [X] Patent Matter [] Trademark Matter

Application Docket No.: 5036-1

Applicant: McKENZIE et al.

Title or Mark: "COMPOSITIONS FOR IMMUNOTHERAPY AND USES THEREOF"

Serial/Reg. No.: 09/163,089

Filed/Issued Date: September 29, 1998

[X] Certificate of Mailing

[] Express Mail No.:

[X] Check for $490.00

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LIST ALL DOCUMENTS BEING SENT TO PATENT OFFICE:

amendment and response after final rejection; request for extension of time

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:

McKENZIE et al.

Serial No.: 09/163,089

Filed: September 29, 1998

Atty. File No.: 5036-1

For: COMPOSITIONS FOR IMMUNOTHERAPY AND USES THEREOF

Group Art Unit: 1645

Examiner: Zeman, R.

AMENDMENT AND RESPONSE
AFTER FINAL REJECTION

CERTIFICATE OF MAILING

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO THE COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450 ON 10/20/04

SHERIDAN ROSS P.C.

BY: Kathleen McCormish

M.S. AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This Amendment and Response is filed in response to a final Office Action having a mailing date of April 26, 2004. Enclosed herewith is a request for a three month extension of time, with the requisite fee, to extend the time for responding from July 26, 2004 to October 26, 2004. No additional fees are believed to be due in connection with this response, but if fees are due, please debit Deposit Account No. 19-1970.

Please amend and reconsider the above-identified application as follows.

Amendments to the Claims are reflected in the Listing of Claims beginning on page 2 of this paper.

Remarks begin on page 6 of this paper.

IN THE CLAIMS:

This Listing of Claims replaces all prior Listings and versions of claims in the above-identified application.

Listing of Claims:

1. (Currently Amended) A composition for eliciting a cellular immune response, comprising isolated mannose receptor-bearing cells and a conjugate comprising ~~an~~ a tumor antigen and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes.

2. (Cancelled)

3. (Original) The composition of Claim 1, wherein said mannose receptor-bearing cells are derived from a cell population selected from the group consisting of peripheral blood leukocytes, bone marrow, stem cells, tumor cells, stromal cells, peritoneal cells, spleen, lung and lymph node cells.

4. (Original) The composition of Claim 1, wherein said mannose receptor-bearing cells comprise cells that are enriched for cells selected from the group consisting of macrophage cells and dendritic cells.

5. (Original) The composition of Claim 1, wherein said mannose receptor-bearing cells comprise cells that express molecules selected from the group consisting of mannose receptor, CD11b, CD14, CD68, CD80 and CD86.

6. (Original) The composition of Claim 1, wherein said mannose receptor-bearing cells are combined with said conjugate *in vitro*.

7. (Original) The composition of Claim 1, wherein said mannose receptor-bearing cells are combined with said conjugate *ex vivo*.

8. (Previously Presented) The composition of Claim 1, wherein said mannose receptor-bearing cells comprise cells that have been contacted with one or more biological response modifiers under conditions effective to induce expression of carbohydrate receptors by said cells.

9. (Previously Presented) The composition of Claim 8, wherein said biological response modifiers induce expression of mannose receptors on a cell capable of expressing said mannose receptors.

10. (Original) The composition of Claim 8, wherein said biological response modifiers are selected from the group consisting of a cytokine and a vitamin.

11. (Previously Presented) The composition of Claim 8, wherein said biological response modifiers are selected from the group consisting of granulocyte macrophage colony stimulating factor (GM-CSF), interleukin-3, interleukin-4, vitamin D, macrophage colony stimulating factor (M-CSF), Flt-3 ligand and tumor necrosis factor (TNF) alpha.

12. (Cancelled)

13. (Previously Presented) The composition of Claim 1, wherein said antigen is a mucin polypeptide, one or more repeated subunits thereof, or an antigenic fragment of said repeated subunits, said fragment comprising at least 5 amino acids of said repeated subunits.

14. (Original) The composition of Claim 13, wherein said mucin is human mucin.

15. (Previously Presented) The composition of Claim 13, wherein said antigen comprises two to eighty copies of said repeated subunits of human mucin.

16. (Original) The composition of Claim 13, wherein said one or more repeated subunits of said antigen comprise part of a fusion polypeptide.

17. (Previously Presented) The composition of Claim 1, wherein said mannose is selected from the group consisting of: (a) mannose and (b) a conformational and configurational isomer of mannose.

18. (Cancelled)

19. (Original) The composition of Claim 1, wherein said composition further comprises a pharmaceutically acceptable carrier.

20. (Currently Amended) A composition comprising a mannose receptor-bearing cell population for eliciting a cellular immune response, wherein said population is derived by culturing mannose receptor-bearing cells with an antigen delivery medium under conditions effective to produce said mannose receptor-bearing cell population, wherein said antigen delivery medium comprises a conjugate comprising ~~an~~ a tumor antigen and a

carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes.

21. (Currently Amended) The composition of Claim 20, wherein said antigen delivery medium comprises a conjugate comprising ~~an~~ a tumor antigen and a carbohydrate polymer comprising mannose selected from the group consisting of fully oxidized mannose comprising free aldehydes and partially reduced mannose having aldehydes.

22. (Cancelled)

23. (Cancelled)

24. (Previously Presented) The composition of Claim 20, wherein said mannose receptor-bearing cell population has been incubated in contact with one or more biological response modifiers prior to said step of culturing.

25. (Previously Presented) The composition of Claim 24, wherein said biological response modifier selected from the group consisting of granulocyte macrophage colony stimulating factor (GM-CSF), interleukin-3, interleukin-4, vitamin D, macrophage colony stimulating factor (M-CSF), Flt-3 ligand and tumor necrosis factor (TNF) alpha.

26. (Original) The composition of Claim 20, wherein said step of culturing is performed *in vitro*.

27-37. (Cancelled)

38. (Previously Presented) A mucin antigen delivery vehicle, comprising an isolated mannose receptor-bearing cell and a conjugate comprising mucin antigen and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes.

39-69. (Cancelled)

70. (Currently Amended) A composition for eliciting a cellular immune response, comprising isolated mannose receptor-bearing cells and a conjugate comprising ~~an~~ a tumor antigen and a carbohydrate polymer comprising mannan, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes.

71-72. (Cancelled)

REMARKS

Claim Amendments:

Claims 1, 20, 21 and 70 have been amended to limit the claimed antigen to a tumor antigen. This amendment is supported by prior Claim 72 (now cancelled) and by the specification on page 22, lines 15-16. Claims 12, 71 and 72 have been cancelled without prejudice to or disclaimer of the subject matter therein. These amendments merely cancel claims or place the claims in a better condition for consideration on appeal, and Applicants submit that the claims are in a condition for allowance. The Examiner's consideration of the same is respectfully requested.

Declaration of Geoffrey Pietersz

Applicants submit herewith a new Declaration under 37 CFR 1.132 of Dr. Pietersz. This Declaration is essentially a "Supplemental Declaration" in that it is a resubmission of the prior Declaration filed on December 18, 2002, except that the issues raised by the Examiner in the April 26 Office Action have been clarified for the record by Dr. Pietersz. This Declaration was not previously submitted in its current form because Applicants and Dr. Pietersz had believed that the prior Declaration was clear and sufficient to present the data. Moreover, this Declaration is submitted only to clarify issues that were raised by the Examiner in response to the first submission of the Declaration. It is believed that this Declaration and the accompanying remarks below address most of the Examiner's final issues and therefore, consideration of this Declaration after final rejection is respectfully requested in the interest of expediting prosecution.

Objection to the Specification and Rejection of Claims 1, 3-17, 19-21, 24-26, 38 and 70-72 Under 35 U.S.C. § 112, First Paragraph:

The Examiner has maintained the prior rejection of claims under 35 U.S.C. § 112, first paragraph, on the basis of enablement. The Examiner acknowledges that the specification is enabling for immunoregulatory compositions comprising mannose-receptor bearing cells and a conjugate comprising MUC1 and a carbohydrate polymer comprising mannose, wherein the carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes. However, the Examiner contends that the specification is not enabling for any antigen as a component of the claimed composition.

Initially, Applicants note that the claims have been amended to expedite prosecution, by claiming only tumor antigens, rather than any antigen. Applicants have provided evidence of the *in vivo* efficacy of the claimed composition using *two different mannose receptor bearing cells*, namely, macrophages (see Examples in specification) and dendritic cells (see December 18 or current Declaration under 37 CFR 1.132 of Dr. Pietersz), and *two different tumor antigens*: mucin, as described in the Examples of the specification, and CRIPTO, which was presented in a Declaration of Geoffrey Pietersz on December 18, 2002 and in the current supplement to that Declaration. Applicants understand that the Examiner has some questions regarding the data from the Pietersz Declaration and Applicants' prior arguments and have tried to address these issues below.

Davis et al.

In the April 26 Office Action, the Examiner first refers to Applicants' prior arguments (summarized in points 1-3 and 7 on page 3 of the April 26 Office Action), and contends that Applicants' arguments and the publication of Davis et al. demonstrate the effects of antigen-conjugate only, reminding Applicants that the mannose receptor bearing cells are part of the claimed composition.

In response to this point, Applicants first refer to Davis et al. and note that this publication describes the pulsing of macrophages with a conjugate comprising oxidized mannan and a parasitic antigen. As taught by the present specification (e.g., see page 15, line 21; page 16, lines 1-3; page 19, lines 5-9; Example 1 and Table 1), a macrophage is a mannose receptor bearing cell and therefore, the experiment in Davis et al. is commensurate in scope with the claimed composition, as Davis et al. contacts these mannose receptor-bearing cells with the oxidized mannan-parasitic antigen conjugate to form the composition of the invention as previously claimed, and then measures the cytokine production by the macrophages as an indicator of a microenvironment conducive to the stimulation of T cell responses. Therefore, the Davis et al. publication is indeed relevant to the issue of the predictability of use of the composition with any antigen. Nonetheless, as discussed above, Applicants have limited the present claims to recite a tumor antigen.

Declaration of Dr. Pietersz under 37 CFR 1.132

The Examiner has also questioned the data presented previously in the Pietersz Declaration. Specifically, the Examiner contends that the Declaration was not clear with regard to whether the mannose portion of the conjugate was oxidized or not because the specification describes both

oxidized and partially reduced mannose. The Examiner has also stated that the CRIPTO data provided in the Declaration is not commensurate in scope with the claimed invention because the data shows *ex vivo* pulsing of dendritic cells with CRIPTO, and that the antigen-polymer conjugate was removed from the dendritic cells prior to administration to mice.

In response to the issue regarding oxidized mannose, Applicants submit herewith the Declaration of Geoffrey Pietersz under 37 CFR 1.132 which, as discussed above, is effectively a supplement to the prior submitted Declaration that attempts to clarify the experimental data for the Examiner. First, as now clearly stated in paragraph 4 of the Declaration, the experiments using the antigen, CRIPTO, were conducted by preparing an antigen-polymer conjugate wherein the mannose was *oxidized*. The conjugate was prepared using essentially the same basic protocol as used for the oxidized-mannan-MUC1 conjugate in the specification, and therefore, the CRIPTO conjugate also meets the limitation of including a fully oxidized carbohydrate polymer comprising free aldehydes.

Second, with regard to the Examiner's contention that the data do not demonstrate a composition that is commensurate in scope with the claims, Applicants respectfully disagree. The composition as presently and previously claimed comprises: "isolated mannose receptor-bearing cells and a conjugate comprising a [tumor] antigen and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes". Applicants believe that the Examiner may not be considering exactly how the composition of the present invention operates and has therefore overlooked the fact that the composition set forth in the Declaration corresponds directly to what is claimed. More particularly, the reason for including the mannose receptor bearing cells in the composition is that the mannose portion of the conjugate binds to the mannose receptors on the cells, and can then be internalized, whereby the attached antigen is processed and presented by the cells to significantly enhance the immune response against the antigen. The advantages of this composition are set forth, for example, in the Summary of the specification. Furthermore, the specification is clear on this point, as set forth on page 12, line 14 to page 13, line 4 of the specification:

> According to the present invention, reference to a composition comprising "carbohydrate receptor-bearing cells and a conjugate comprising an antigen and oxidized carbohydrate" or "carbohydrate receptor-bearing cells contacted with a conjugate comprising an antigen and oxidized carbohydrate" can encompass one or

more of: (1) a mixture of conjugate and receptor-bearing cells wherein the conjugate is not bound to the cells; (2) a mixture of conjugate and receptor-bearing cells wherein the conjugate is bound to the cells, but not yet internalized; (3) receptor-bearing cells wherein the conjugate has been internalized; (4) receptor-bearing cells wherein the conjugate has been internalized and processed; and/or (5) receptor-bearing cells wherein the conjugate has been internalized, processed and presented.

Therefore, in the case of the "washing step" referenced in the Declaration and of concern to the Examiner, only free (unbound) conjugate would have been washed away. The composition that was administered to the mice still comprises both the conjugate and the mannose receptor bearing cells, because the conjugate, after being contacted with (combined with, pulsed with) the mannose receptor bearing cells, will bind to the cells via the mannose receptors, and then at least some of the conjugate will have been internalized by the cells for processing after 2 hours of pulsing (e.g., scenarios (2)-(4) in the quotation from the specification above). As stated in the specification and as previously argued by Applicants, among the advantages of the present composition are the ability of the conjugate to avoid recognition by naturally occurring antibodies *in vivo* and even more importantly, the ability of the conjugate to be delivered to the MHC Class I pathway for significant enhancement of T cell responses against the antigen. Washing away from the composition of any excess free, unbound conjugate can further enhance these advantages by reducing the likelihood of free conjugate cross-reacting with the naturally occurring antibodies *in vivo* (e.g., Gal). These advantages are achieved by the special components of the invention in combination. These advantages do not need to be recited in the claims as they are inherent features of the combining of the recited mannose receptor bearing cells with the recited antigen conjugate that includes mannose, wherein the carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes (i.e., the mechanism by which the composition operates illustrates the advantages of the invention).

The claimed invention is a composition that has been demonstrated first in the specification by working examples using one combination of mannose receptor bearing cell (macrophage) and a tumor antigen (MUC1), and again using a different mannose receptor bearing cell type (dendritic cell) and different tumor antigen (Cripto) in the Declaration of Dr. Pietersz. In both the specification and the Declaration, *in vivo* efficacy using the claimed composition was demonstrated. The claims do not require that the components of the composition be separate from one another, as the Examiner

seems to imply, and indeed, once combined into a composition as claimed, the components will begin to associate with one another via the binding of the mannose component to the mannose receptors on the cells.

Therefore, Applicants submit that the composition set forth in the present claims, as amended, are fully enabled by the specification, as evidenced by the additional experimental data provided by Dr. Pietersz Declaration. In view of these remarks, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1, 3-17, 19-21, 24-26, 38 and 70-72 under 35 U.S.C. § 112, first paragraph.

Objection to the Claims:

The Examiner has objected to Claim 71 as being a substantial duplicate of Claim 70. To expedite prosecution, Applicants have cancelled Claim 71 without prejudice to or disclaimer of the subject matter therein.

Applicants have attempted to respond to all of the issues raised by the Examiner in the April 16, 2004 Office Action, and in a manner in accordance with 37 CFR 1.116. Therefore, Applicants submit that the claims are in a condition for allowance and respectfully request that if the Examiner has any further concerns with regard to the claims, that he consider contacting the below-named agent at (303) 863-9700 to expedite prosecution.

Respectfully submitted,

SHERIDAN ROSS P.C.

By: Angela Sebor

Angela Dallas Sebor
Registration No. 42,460
1560 Broadway, Suite 1200
Denver, CO 80202-5141
(303) 863-9700

Date: October 20, 2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:	)	Group Art Unit: 1645
McKENZIE et al.	)	Examiner: Zeman, R.
Serial No.: 09/163,089	)	
Filed: September 29, 1998	)	DECLARATION OF GEOFFREY A PIETERSZ (37 CFR 1.132)
Atty. File No.: 5036-1 (formerly 4102-1)	)	
For: COMPOSITIONS FOR IMMUNOTHERAPY AND USES THEREOF	)	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Geoffrey A. Pietersz, declare as follows:

1. I am a co-inventor of the above-referenced patent application and am familiar with the application. I am a skilled artisan in the field of immunology/chemistry.

2. This Declaration is being submitted in conjunction with an Amendment and Response to the Office Action having a mailing date of April 26, 2004.

3. The following discussion is provided in traverse of the Examiner's rejection of Claims 1, 3-17, 19-21, 24-26, 38 and 70-72 under 35 U.S.C. § 112, first paragraph.

4. This Declaration is provided as a Supplement to the Declaration under 37 CFR 1.132 previously submitted in the above-identified application on December 18, 2002, and provides more detail regarding the previously described experiments as they relate to the claimed invention. Specifically, the following data demonstrate the use of isolated mannose receptor-bearing cells and a conjugate comprising a tumor antigen (where the antigen is non-Muc1) and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes, to induce cellular immune responses in animals *in vivo*.

Dendritic Cells (the isolated mannose receptor-bearing cells)

H-2K^b C57BL/6 female 6-8 week old mice were used in the experiments. Mice were bred at the Austin Research Institute Biomedical Animal Research Lab

Bone marrow cells from C57BL/6 female mice were cultured at 10^6 cells/ml in tissue culture. Petri dishes contained RPMI 1640 medium (Gibco, NY, USA) supplemented with 1000 units/ml granulocyte and macrophage colony stimulating factor (GM-CSF), 10 μg/ml of interleukin-4 (IL-4), 10% heat inactivated fetal calf serum (FCS), 4mM L-glutamine, 100 U/ml penicillin, 100 :g/ml streptomycin sulphate and 100mM β-mercaptoethanol. At day 6 cells showed markers of mature dendritic cells (DCs), and expression of the mannose receptors

***Ex vivo* Treatment of Dendritic Cells with Oxidised Mannan-Antigen Conjugates to Produce the Composition Comprising Isolated Mannose Receptor-bearing Cells and a Conjugate Comprising a Tumor Antigen and a Carbohydrate Polymer Comprising Oxidised Mannose**

The mannose receptor-bearing dendritic cells as described above were washed, resuspended in the same culture media at $1x10^6$ cells/ml. A conjugate of oxidized mannan-Cripto, prepared as described for the oxidized mannan-MUC1 conjugates described in the present application (see Example 1), was loaded on to the DCs for 2 hours by adding the conjugate to the culture medium. This resulted in the generation of Cripto Pulsed DCs

Cripto is a protein expressed in embryonic and cancer cells. It is not expressed in normal tissues. The sequence of CRIPTO used here is a 17-mer peptide that is identical in both human and mouse CRIPTO. The sequence is: CPPSFYGRNCEHDVRKE, and is an antigenic portion of the Cripto protein.

Cripto Pulsed DCs were then washed thoroughly, resuspended at $1x10^7$cells/0.5ml in PBS (phosphate buffered saline) and 50 :l was injected intradermally in mice in the hind footpads. 10 days later mice were boosted. The pulsed DC's as described above meet the limitations of the composition of the invention as set forth in the present application on page 12, line 14 to page 13, line 4, because the pulsed DC's, even after washing, can include: (1) a mixture of conjugate and receptor-bearing cells wherein the conjugate is bound to the cells, but not yet internalized; (2) receptor-bearing cells wherein the conjugate has been internalized; (3)

receptor-bearing cells wherein the conjugate has been internalized and processed; and/or (4) receptor-bearing cells wherein the conjugate has been internalized, processed and presented.

Antigen Recall in Mice Treated with Pulsed Dendritic Cells

After 10-14 days, mice were sacrificed and splenocytes were isolated. Antigen recall (to measure the ability of the administered DCs to stimulate the immune response *in vivo* upon infection by an antigen) was assessed by ELISPOT IFN-gamma assays (which are a measure of T cell immune response) after addition of test or control antigens.

The test antigen was the Cripto 17-mer epitope described above. The control antigen was from an epitope comprising the Variable Number of Tandem Repeats (VNTR) of amino acid residues from Mucin1 (Muc1), a protein expressed on various tumour cells. In addition, a positive control consisting of ConA was used.

The results are shown in the attached figures.

As can be seen from the figures, producing a composition as claimed in the present application by pulsing DCs with a conjugate comprising oxidized mannan-Cripto in accordance with the invention described in the present application, and administration of the pulsed cells (i.e., the composition) to animals, resulted in *in vivo* stimulation of IFN-gamma by the 17-mer Cripto peptide (i.e there is antigen recall). The degree of stimulation was comparable with the response to Con A, the positive control, but substantially higher than the control where immune cells were not exposed to any antigens (indicated by a "-" under the histogram at the extreme right in each of the figures).

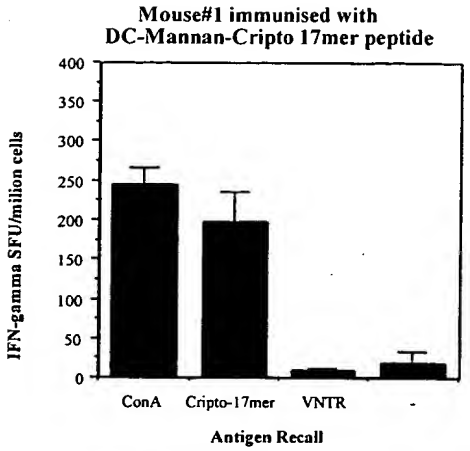
The antigen recall of the 17-mer Cripto peptide was also substantially greater than with VNTR, indicating a specific antigen selection and presentation by APCs, and leading to generation of a T cell immune response to the Cripto peptide *in vivo*.

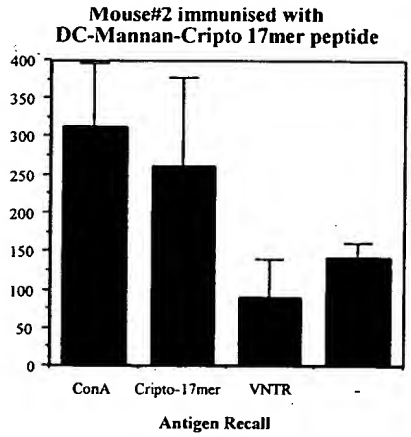
In conclusion, the results show that the Cripto 17 mer peptide, a cancer antigen that is distinct from Muc1, can stimulate DCs *ex vivo* when conjugated with mannan, enabling the pulsed DCs to stimulate T cell immune response to the antigen *in vivo* following administration.

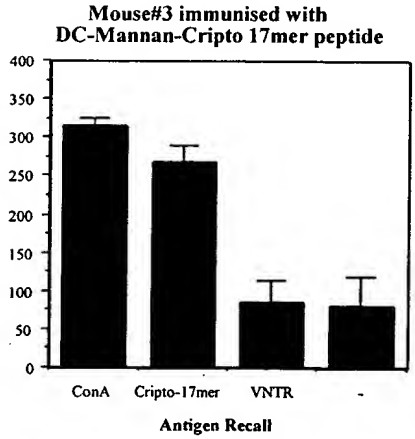
5. I hereby declare that all statements made herein of my own are true and that all statements made on information and belief are believed to be true; and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and

that such willful false statements may jeopardize the validity of the subject application or any patent issuing therefrom.

Date: 20/10/04 By: G. A Pietersz
Geoffrey A. Pietersz







Initial: km

Date 10/20/04

PTO Stamp indicates receipt of: [X] Patent Matter [] Trademark Matter

Application Docket No.: 5036-1

Applicant: McKENZIE et al.

Title or Mark: "COMPOSITIONS FOR IMMUNOTHERAPY AND USES THEREOF"

Serial/Reg. No.: 09/163,089

Filed/Issued Date: September 29, 1998

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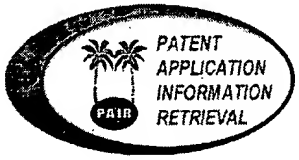
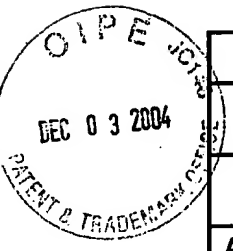
LIST ALL DOCUMENTS BEING SENT TO PATENT OFFICE:

amendment and response after final rejection; request for extension of time

United States Patent and Trademark Office

PATENT APPLICATION INFORMATION RETRIEVAL





Search results as of: 11-30-2004::15:47:3 E.T.

Search results for application number: 09/163,089			
Application Number:	09/163,089	Customer Number:	22442
Filing or 371(c) Date:	09-29-1998	Status:	Abandoned -- Failure to Respond to an Office Action
Application Type:	Utility	Status Date:	11-01-2004
Examiner Name:	ZEMAN, ROBERT A	Location:	ELECTRONIC
Group Art Unit:	1645	Location Date:	-
Confirmation Number:	9586	Earliest Publication No:	-
Attorney Docket Number:	5036-1	Earliest Publication Date:	-
Class/ Sub-Class:	424/185.1	Patent Number:	-
First Named Inventor:	IAN F. C. MCKENZIE, BRUNSWICK, (AU)	Issue Date of Patent:	-
Title Of Invention:	COMPOSITIONS FOR IMMUNOTHERAPY AND USES THEREOF		

Search Options

Assignments
Continuity Data
Image File Wrapper

File History	
Date	Contents Description
11-03-2004	Mail Abandonment for Failure to Respond to Office Action
11-01-2004	Abandonment for Failure to Respond to Office Action
10-27-2004	Workflow incoming amendment IFW
04-26-2004	Mail Final Rejection (PTOL - 326)
04-23-2004	Final Rejection
01-14-2004	IFW Amended case processing Complete
01-14-2004	Date Forwarded to Examiner
11-25-2003	Response after Non-Final Action
11-25-2003	Request for Extension of Time - Granted
07-28-2003	Mail Examiner Interview Summary (PTOL - 413)
07-21-2003	Examiner Interview Summary Record (PTOL - 413)
05-19-2003	Mail Non-Final Rejection
05-19-2003	Non-Final Rejection

03-11-2003	Date Forwarded to Examiner
03-11-2003	Date Forwarded to Examiner
02-03-2003	Request for Continued Examination (RCE)
03-11-2003	Express Abandonment (for Entry of CPA / RCE / Rule129)
03-04-2003	Petition to Revive Application - Granted
02-03-2003	Petition Entered
02-03-2003	Workflow - Request for RCE - Begin
12-18-2002	Affidavit(s) (Rule 131 or 132) or Exhibit(s) Received
12-26-2002	Mail Advisory Action (PTOL - 303)
12-24-2002	Advisory Action (PTOL-303)
11-27-2002	Affidavit(s) (Rule 131 or 132) or Exhibit(s) Received
12-09-2002	Date Forwarded to Examiner
11-27-2002	Amendment after Final Rejection
11-27-2002	Request for Extension of Time - Granted
07-29-2002	Mail Final Rejection (PTOL - 326)
07-29-2002	Final Rejection
04-04-2002	Information Disclosure Statement (IDS) Filed
04-12-2002	Date Forwarded to Examiner
04-08-2002	Response after Non-Final Action
04-08-2002	Request for Extension of Time - Granted
12-03-2001	Case Docketed to Examiner in GAU
12-03-2001	Case Docketed to Examiner in GAU
12-02-2001	Case Docketed to Examiner in GAU
11-12-2001	Case Docketed to Examiner in GAU
10-23-2001	Mail Non-Final Rejection
10-22-2001	Non-Final Rejection
08-09-2001	Date Forwarded to Examiner
08-03-2001	Response to Election / Restriction Filed
08-03-2001	Request for Extension of Time - Granted
06-08-2001	Mail Restriction Requirement
06-07-2001	Requirement for Restriction / Election
06-06-2001	Case Docketed to Examiner in GAU
05-16-2001	Date Forwarded to Examiner
05-14-2001	Amendment after Final Rejection
02-13-2001	Mail Final Rejection (PTOL - 326)
02-08-2001	Final Rejection
01-16-2001	Date Forwarded to Examiner
01-02-2001	Response after Non-Final Action
01-02-2001	Request for Extension of Time - Granted
07-28-2000	Mail Non-Final Rejection
07-28-2000	Non-Final Rejection
07-05-2000	Date Forwarded to Examiner
06-30-2000	Response to Election / Restriction Filed

06-05-2000	Mail Restriction Requirement
06-05-2000	Requirement for Restriction / Election
04-06-2000	Date Forwarded to Examiner
03-27-2000	Response to Election / Restriction Filed
10-28-1999	Information Disclosure Statement (IDS) Filed
02-29-2000	Mail Restriction Requirement
02-28-2000	Requirement for Restriction / Election
02-23-1999	Case Docketed to Examiner in GAU
01-21-1999	Application Dispatched from OIPE
01-19-1999	Application Is Now Complete
11-16-1998	Notice Mailed--Application Incomplete--Filing Date Assigned
11-03-1998	IFW Scan & PACR Auto Security Review
10-21-1998	CRF Is Good Technically / Entered into Database
10-02-1998	CRF Disk Has Been Received by Preexam / Group / PCT
10-02-1998	Initial Exam Team nn

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:) Group Art Unit: 1645
)
McKENZIE et al.) Examiner: Zeman, Robert A.
)
Serial No.: 09/163,089) NOTICE OF APPEAL
)
Filed: September 29, 1998)
)
Atty. File No.: 5036-1)
)
For: "COMPOSITIONS FOR IMMUNOTHERAPY AND USES THEREOF")
)

CERTIFICATE OF MAILING

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO THE COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450 ON 10/26/04.

SHERIDAN ROSS P.C.

BY: Kathleen McGinnis

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313

Dear Sir:

Applicant hereby appeals to the Board of Appeals from the decision of the Examiner mailed April 26, 2004, finally rejecting Claims 1, 3-17, 19-21, 24-26, 38 and 70-72. Enclosed herewith is a check in the amount of $170 for the Notice of Appeal fee specified in 37 CFR §1.17(b).

A petition for an extension of time under 37 CFR §1.136, with the appropriate fee, was submitted with the Amendment and Response After Final Rejection extending the time for response from July 26, 2004, to October 26, 2004. Accordingly, the Notice of Appeal is believed to be timely and no additional fee is believed to be required. Please credit any overpayment or debit any underpayment to Deposit Account 19-1970.

Respectfully submitted,

SHERIDAN ROSS P.C.

By: Gary J. Connell

Gary J. Connell
Registration No. 32,020
1560 Broadway, Suite 1200
Denver, CO 80202-5141
(303) 863-9700

Date: Oct. 26, 2004

SHERIDAN ROSS P.C.
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(303) 863-9700

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DENVER, CO 80274
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COMMISSIONER OF PATENTS AND TRADEMARKS

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SHERIDAN ROSS

VENDOR NO. VENDOR NAME 22598

TRANSACTION DATE	REFERENCE	GROSS AMOUNT		DEDUCTION	NET AMOUNT
10/22/04	OPER-KB	Notice of Appeal Filing Fee	5036-1	1122000	170.00

CHECK DATE	CHECK NO.	TOTAL GROSS	TOTAL DEDUCTION	CHECK AMOUNT
10/22/04	22598			170.00

Initial: km

Date 10/26/04

PTO Stamp indicates receipt of: [X] Patent Matter [] Trademark Matter

Application Docket No.: 5036-1

Applicant: McKENZIE et al.

Title or Mark: "COMPOSITIONS FOR IMMUNOTHERAPY AND USES THEREOF"

Serial/Reg. No.: 09/163,089

Filed/Issued Date: September 29, 1998

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Initial: km

PTO Stamp indicates receipt of:

Application Docket No.: 5036-1 [X] Patent Matter Date 10/26/04

Applicant: McKENZIE et al. [] Trademark Matter

Title or Mark: "COMPOSITIONS FOR IMMUNOTHERAPY AND USES THEREOF"

Serial/Reg. No.: 09/163,089

Filed/Issued Date: September 29, 1998

[X] Certificate of Mailing

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[X] Check for $ 170.00

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notice of appeal

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